

**Final Report for
FY 2004 Award
October 2006**

Project Title: *Early Detection of Melanoma and other Cancers in Residents of Nevada*

Grant No.: *DE-FG02-04ER63863*

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Project Description:

The overall goal of this project was to develop simple and inexpensive tests to screen for the presence of early stage cancer in the residents of Nevada with a particular emphasis on the membership of the Hotel Employee Restaurant Employee International Union (HEREIU) in Las Vegas. Our specific goals were:

- 1) to develop a clinical database of individuals with cancer and to create a biological specimen Collection and Storage Systems (the NVCi bio-bank);
- 2) to initiate screening of individuals for proteomic markers indicating susceptibility to or the presence of specific cancers, e.g. breast, ovarian, prostate and bladder. In addition, we proposed the implementation of novel digital imaging technologies to detect melanoma;
- 3) to genotype blood samples from individuals who consent to participate in IRB approved research studies using a high throughput single nucleotide polymorphisms (SNP) method based on optical thin-film biosensor chip technology; and
- 4) to conduct biostatistical analysis of clinical, demographic, genetic, proteomic and digital imaging data to stratify the population cohort into relative risk groups for cancers that are prevalent in Nevada.

Summary Project Report:

Specific Aim 1: *Clinical Database development, Sample Collection and Storage*

Considerable progress was made in this objective during the funding period. The HEREIU has a self-insured health plan that covers ~125,000 union employees and their family members. They provided the Nevada Cancer Institute (NVCi), via a

Memorandum of Agreement, access to the health records of all insured individuals and authority to develop programs that focus on early stage detection of cancers, outreach and education and patient navigation. We utilized DOE funds to provide partial support for the development of a relational database that contains information on all individuals who were diagnosed with cancer between 1998 and 2002, how they were treated and what were the clinical outcomes. This database provided baseline information by which the effectiveness of NVCi-HEREIU cancer navigation/education and intervention programs will be measured in the future. In addition, comparison with data in the Nevada State cancer Registry, housed at NVCi, has identified discrepancies in the frequency of certain cancers between union members and the general population of Nevada. Specifically, this study demonstrated that the frequency of breast cancer in the HEREIU cohort was 30% higher than in the state at large and that the rates of screening test, such as mammography and PAP smears, were considerable less than the national average. These observations provided a strong incentive to establish a mobile mammography, phlebotomy and cancer screening unit, termed the Hope Coach, which will become operational in early 2007.

Utilizing funds provided by the DOE, we have established the resources and infrastructure needed to create a blood, urine and tissue banking facility at NVCi that will be collecting biological samples from patients who have consented to participate in IRB approved clinical trials at NVCi. Since our clinical and research building opened to the public in September of 2005, samples from over 400 patients have been banked for research on cancer genetics and proteomic biomarker discovery. To facilitate this ongoing enterprise, we have purchased multiple -80°C freezers with independent alarm monitors for sample storage, barcode printers and scanners, a Freezer Works™ software system for maintenance of sample inventory and interfacing with the NVCi Electronic Medical Record database operational under the IMPAC control system. Personnel have been trained in safety issues; sample collection protocols, ascertainment of informed consent and standard operating procedures for processing and storing patient samples have been implemented.

We also purchased/leased state-of-the-art equipment which was available to all NVCi faculty and their collaborators as core facilities. These items included a Bio-Rad Luminex instrument for multiplex ELISA immunoassays using flow-sorted micro spheres, a Zymark robotic liquid handling system for high throughput processing of biological samples, a Genetix microarray printer for the preparation of investigator-designed oligonucleotide and protein arrays, a processor for the preparation of tissue microarrays for immunohistochemical analysis of potential biomarkers and three dual 384-head PCR machines for high throughput genotyping.

Specific Aim 2: *Clinical Screening*

It was our original intention to utilize the resources outlined above to provide early stage cancer detection screening services to study volunteers from the HEREIU. Unfortunately, a definitive agreement between NVCi and the HEREIU as to where and when screening activities would be conducted was not concluded during the DOE funding period. However as noted above, NVCi, in partnership with HEREIU and

corporate backers, will be implementing the mobile Hope Coach program in early 2007. This will provide a mechanism to provide mammography, chest x-rays and blood and/or urine based cancer diagnostic tests on an ongoing basis. It is anticipated that screening for breast, ovarian, prostate, lung and bladder cancer will be initiated in the near future. For technical reasons, our plan to screen for early stage melanoma using digital imaging technologies has been abandoned.

Specific Aim 3: *Genetic Analysis*

Our original objective was to establish a high throughput SNP technology that could be used to genotype cancer-relevant genes from selected NVC patient samples collected for the Bio-Bank. We established a SNP typing capability that was based on robotic array printing on optical thin-film clips. However, because of the significant improvements in SNP technology made by the commercial sector during the past two years, it is now most economical to conduct large scale SNP studies through contracts with a commercial provider. Two SNP screening studies to identify biomarkers for cardiovascular disease and population based haplotype analysis for cancer susceptibility have been subcontracted to Illumina and over 7.5 million genotypings have been determined to date.

Specific Aim 4: *Biostatistical Analysis*

Our utilization of biostatistical analysis has so far been limited to an ongoing study of serum-protein biomarkers for the early detection of ovarian cancer, a project that was initiated with DOE funding. Both univariate and multivariate statistical analytical tools have been established for this and other projects. The latter include support vector machines, three nearest neighbors, classification trees, e.g. Random Forest and Logistic Regression methods.

In conclusion, the direct and indirect funds provided by the DOE FY2004 earmark (DE-FG02-04ER63863) have provided the resources and infrastructure to create state-of-the-art facilities to bank biological specimens and to conduct genomic and proteomic research related to the diagnosis, progression and therapy of cancer.